

USPT	l22 same (l15 or l16 or l9) same l10	1	L24
USPT	l22.ti,ab,clm. and (l15 or l16 or l8 or l9) and l10	9	L23
USPT	multivalent or multi-valent or polyvalent or poly-valent or multicomponent or multi-component or polycomponet or poly-component	34605	L22
USPT	('5106616')[PN]	1	L21
USPT	l19 and l17 not l18	64	L20
USPT	l10 same (virus or viral)	500	L19
USPT	l17 same l10	4	L18
USPT	l16 or l9	27496	L17
USPT	quila or quil or quil-a	352	L16
USPT	quila or quil	352	L15
USPT	l13 and l9	29	L14
USPT	l10.ti,ab,clm.	573	L13
USPT	l11 and (viral or virus)	145	L12
USPT	l9 and l10	245	L11
USPT	clostrid\$ or dysent\$	4295	L10
USPT	(aq-7 or qa-17 or qa-18 or qa-18 or qa-21 or qa-21v1 or qa21v1 or qa21v2 or qa-21v2 or sapon\$ or quinoa or qs-l1 or qsl1 or quillaja or triterpene)	27407	L9
USPT	(aq-7 or qa-17 or qa-18 or qa-18 or qa-21 or qa-21v1 or qa21v1 or qa21v2 or qa-21v2 or sapon\$ or quinoa or qs-l1 or qsl1 or quillaja or triterpene) and clostrid\$	201	L8
USPT	saponin\$.ti.	46	L7
USPT	(l4 or l5) and l3 and (l1 or l2)	2	L6
USPT	clostrid\$.clm.	395	L5
USPT	clostri\$.clm.	417	L4
USPT	(quila or quil-a or sapon\$).clm.	2768	L3
USPT	(respirator\$ or lung\$ or aveol\$).clm.	5712	L2
USPT	(viral or virus).clm.	8320	L1

WEST

Generate Collection

L20: Entry 44 of 64

File: USPT

Jul 16, 1996

DOCUMENT-IDENTIFIER: US 5536496 A

TITLE: Pasteurella multocida toxoid vaccines

BSPR:

Still other preferred vaccine compositions of this invention result from combining the free toxoid and/or the bacterin-toxoid of this invention with other vaccinal agents. An illustrative example is a vaccine composition formed by the combination of a whole cell *B. bronchiseptica* bacterin with the *P. multocida* bacterin-toxoid. Alternatively, the *P. multocida* bacterin-toxoid is illustrated in further combination with *E. rhusiopathiae*. Other possible vaccinal agents which may be combined with the vaccine components of this invention include, without limitation, *Escherichia coli*, *Streptococcus suis*, *Mycoplasma hyopneumoniae*, *Actinobacillus pleuropneumoniae*, *Clostridium perfringens* types C and D toxoids, *Pseudorabies Virus Vaccine* (modified live virus and/or killed virus), *Rotavirus Vaccine* (modified live virus), *Coronavirus Vaccine* (modified live virus).

BSPR:

Alternatively or additionally, the free toxoid and/or bacterin-toxoid can be admixed or adsorbed with a conventional adjuvant. The adjuvant is used as a non-specific irritant to attract leukocytes or enhance an immune response. Such adjuvants include, among others, amphigen, aluminum hydroxide, muramyl dipeptide, and saponins such as Quil A.

DEPR:

Alternatively, the bacterin toxoid may be employed in vaccine compositions with other vaccine components. For example, the suspension of adsorbed *P. multocida* is mixed with equal volumes of similarly adsorbed and preserved cultures of *Bordetella bronchiseptica* and *Erysipelothrix rhusiopathiae* to make a bacterin-toxoid vaccine, referred to as Atrobac 3 (Beecham Laboratories), which has a dose volume of 2 ml. Whether the bacterin-toxoid is used alone or in combination, saponin (0.5 mg/ml) may be added as adjuvant.

WEST

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L20: Entry 49 of 64

File: USPT

Apr 21, 1992

DOCUMENT-IDENTIFIER: US 5106616 A
TITLE: Administration of acemannan

BSPR:

Aloe vera is not a cactus plant, as widely believed, but rather a member of the lily family. There are about 360 species of aloe plants known. Harding, Aloes of the World: A Checklist, Index and Code, Excelsa 9: 57-94 (1979). They seem to thrive in hot, arid areas and are widely scattered from the Mediterranean Sea, Middle East, Africa, China, Japan, Mexico and the southern U.S.A. A few of the important species used for their medicinal properties are Aloe barbadensis Miller (aloe vera), A. arborescens, A. plicatilis, A. vahombe, A. saponaria, A. africana, A. ferox and Aloe perryi. Reynolds, Aloes of Tropical Africa and Madagascar, The Trustees, The Aloe Book Fund, Mbabane Swaziland. However, A. barbadensis Miller is generally recognized as the "true aloe" because of its wide use and, reportedly, most effective healing power, although in Japan, A. arborescens Miller traditionally has been used as a folk remedy for various ailments ranging from gastrointestinal disorders to athlete's foot.

DEPR:

Acemannan's second expected use is as an adjuvant wherein the Carrisyn.TM. extract may promote the response to any inactivated vaccine containing viral, parasitic or bacterial antigens including the following: cattle vaccines --infectious bovine rhinotracheitis, parainfluenza 3, respiratory syncytial virus, bovine virus diarrhea, rotavirus, coronavirus, bluetongue, rabies, clostridial diseases, footrot, pinkeye, anaplasmosis, babesiosis, pasteurellosis, salmonellosis, colibacillosis, corynebacterium sp., vibriosis, brucellosis, leptospirosis, hemophilus somnus, foot and mouth disease, papillomavirus, and staphylococcal mastitis; sheep vaccines--clostridial diseases, footrot, rabies, foot and mouth disease, erysipelas, louping ill, and caseous lymphadenitis; swine vaccines--parvovirus, erysipelas, transmissible gastroenteritis, pseudorabies, bordetella bronchiseptica, colibacillosis, pasteurellosis, foot and mouth disease, clostridial diseases, leptospirosis, and hemophilus pleuropneumonia; equine vaccines--influenza, rhinopneumonitis, tetanus, strangles, equine arteritis, Eastern, Western and Venezuelan encephalitis, and rabies; feline vaccines--rhinotracheitis, feline leukemia, calicivirus, chlamydiosis, lentivirus, panleukemia, rabies, and infectious peritonitis; canine vaccines--distemper, adenovirus (types 1 and 2), rabies, parvovirus, leptospirosis, parainfluenza, coronavirus, measles, rhodococcus equi, tetanus, and rabies; and avian vaccines--infectious bursal disease, Newcastle disease, infectious bronchitis, infectious laryngotracheitis, Mareks disease, and coccidiosis.

WEST

Generate Collection

Search Results - Record(s) 1 through 5 of 5 returned.**1. Document ID: US 6083512 A**

L29: Entry 1 of 5

File: USPT

Jul 4, 2000

DOCUMENT-IDENTIFIER: US 6083512 A

TITLE: Multicomponent clostridial vaccines using saponin adjuvants**ABPL:**

Novel multicomponent clostridial vaccine formulations using readily dispersible, non-depot adjuvants, such as saponin, are disclosed. The vaccines can be administered to cattle intramuscularly or subcutaneously without the severe persistent local reactions, such as granulomas, abscesses, and scarring, normally seen with other multicomponent clostridial vaccines.

BSPR:

The present invention relates generally to vaccine compositions and methods of using the same. More specifically, the invention pertains to multicomponent clostridial vaccines made without stabilizing carriers or depot adjuvants, but rather with a readily dispersible, water-soluble adjuvant, saponin.

BSPR:

Saponins are glycosidic natural plant products, grouped together based on several common properties. The saponins are surfactants, a characteristic illustrated by their tendency to foam when shaken. Saponins are able to lyse red blood cells, form complexes with cholesterol and are toxic to fish. Saponins have been employed as adjuvants in a number of vaccine compositions including vaccines against protozoal infections (U.S. Pat. No. 4,767,622), canine distemper vaccines (U.S. Pat. No. 5,178,862), vaccines against foot and mouth disease, among others. Awad et al. (1986) Assiut Vet. Med. J. 17:201-214 describe a comparison of single component blackleg vaccines including either alum, aluminum gel with saponin or oil adjuvants. However, the use of soluble adjuvants that are readily dispersed from the injection site, and have no depot effect, such as saponin, with a multicomponent clostridial vaccine, has not heretofore been described.

BSPR:

The present invention is based on the surprising discovery that the water-soluble adjuvant, saponin, can be used in place of a depot adjuvant in multicomponent clostridial vaccines for cattle. The vaccines are safe and nontoxic.

BSPR:

Accordingly, in one embodiment, the invention is directed to a multicomponent clostridial vaccine composition comprising two or more clostridial immunogens and a dispersible, soluble adjuvant.

BSPR:

In another embodiment, the subject invention is directed to a multicomponent clostridial vaccine composition comprising:

BSPR:

In yet another embodiment, the invention is directed to a multicomponent clostridial vaccine composition comprising:

BSPR:

A "multicomponent" clostridial vaccine composition refers to a vaccine derived from cultures of two or more serotypes of the same clostridial species and/or cultures derived from different clostridial species. A multicomponent vaccine

will generally be derived from 2 to 15 different serotypes or species, more usually 2 to 10 different serotypes or species, depending on the diseases in question and the subject being treated.

BSPR:

Central to the present invention is the surprising discovery that stable, potent, multicomponent clostridial vaccines can be made without the use of depot adjuvants. In particular, the present invention provides for vaccines including rapidly dispersed, soluble adjuvants, that is, adjuvants that are not retained at the injection site for a significant period of time, thereby exhibiting low tissue reactivity. The vaccines can be administered intramuscularly and subcutaneously without the harmful side effects and chronic inflammatory responses that produce granulomas and abscesses, seen with other clostridial vaccine compositions when administered via these routes.

BSPR:

The vaccines are polyvalent, that is, they are derived from cultures of two or more clostridial serotypes and/or from different species of *Clostridium*. Accordingly, the immunogens can be derived from any of the clostridial species and serotypes thereof, depending on the disease or diseases targeted, such as, but not limited to *C. perfringens*; *C. septicum*; *C. tetani*; *C. chauvoei*; *C. novyi*; *C. sordellii*; *C. haemolyticum*; *C. botulinum*; and serotypes of these species.

BSPR:

Of particular interest, are multicomponent vaccine compositions derived from bacterins of *C. chauvoei* and toxoids of *C. haemolyticum*, *C. chauvoei*, *C. septicum*, *C. novyi*, *C. sordellii* and *C. perfringens*, Types C and D. Such a multicomponent vaccine composition is termed an "8-way" vaccine herein because it provides immunity not only against the specific organisms identified, but also against *C. perfringens*, Type B. Another particularly preferred vaccine contains the same fractions as above, with the exception of *C. haemolyticum* and, hence, is referred to as a "7-way" vaccine.

BSPR:

Non-clostridial antigens may also be added to the vaccines to afford protection against a wide spectrum of diseases. For example, antigens derived from *Moraxella bovis*, *Haemophilus somnus*, *Pasteurelia hemolytica*, various respiratory viruses, as well as others, can be added to the multicomponent clostridial vaccine compositions of the present invention for use bovine subjects.

DEPR:

A 7-way multicomponent clostridial vaccine was prepared as described in Example 1, except that the *C. haemolyticum* component was not included in the formulation. This vaccine was compared with an identical vaccine with no adjuvant, as well as with a commercially available multicomponent clostridial vaccine, Ultrabac 7 (SmithKline Beecham), which includes 25% Al(OH)₃ gel as adjuvant, in studies of local reactions in cattle, antibody responses in cattle, and antibody responses and protection against an infective challenge in guinea-pigs.

DEPR:

Thus, novel multicomponent clostridial vaccine compositions using saponin adjuvants, and methods for administering the same, are disclosed. Although preferred embodiments of the subject invention have been described in some detail, it is understood that obvious variations can be made without departing from the spirit and the scope of the invention as defined by the appended claims.

DEPC:

Preparation of an 8-way Multicomponent Clostridial Vaccine Including a Saponin Adjuvant

DEPC:

Potency of the Multicomponent Clostridial Vaccine

DEPC:

Preparation of a 7-Way Multicomponent Clostridial Vaccine Including a Saponin Adjuvant

CLPR:

1. A multicomponent clostridial vaccine composition, consisting of immunogens from two or more species or serotypes of Clostridium, a saponin adjuvant, and a pharmaceutically acceptable carrier.

CLPR:

16. A multicomponent clostridial vaccine composition, consisting of immunogens from two or more species or serotypes of Clostridium, a saponin adjuvant, a pharmaceutically acceptable carrier, and a preservative.

CLPR:

19. A multicomponent clostridial vaccine composition, consisting of immunogens from two or more species or serotypes of Clostridium, and a saponin adjuvant.

ORPL:

Thomson et al., 1969, "Immunogenicity of a multicomponent clostridial oil emulsion vaccine in sheep", Vet. Rec., 85:81-85 (1969).

ORPL:

Sterne et al., 1962, "Immunisation of sheep with multi-component clostridial vaccines", Vet. Rec., 74(34):909-913.

Full	Title	Citation	Front	Review	Classification	Date	Reference	Claims	KWIC	Draw Desc	Image
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2. Document ID: US 5965375 A

129: Entry 2 of 5

File: USPT

Oct 12, 1999

DOCUMENT-IDENTIFIER: US 5965375 A

TITLE: Diagnostic tests and kits for Clostridium difficile

DEPR:

To obtain other suitable molecular tag/capture moiety pairs for which binding is reversible under mild conditions, one can screen for peptides that bind a given molecular tag by, for example, enrichment of display libraries, including phage display libraries. A particularly useful method by which to obtain such reversibly binding molecular tag/capture moiety pairs is described in co-filed U.S. patent application Ser. No. 08/832,985 (filed Apr. 4, 1997). This method involves enriching conventional display libraries for members displaying more than one copy of a display polypeptide prior to affinity screening of such libraries with a target of interest, such as a molecular tag. The rationale for this method is believed to be that affinity binding of library members to an immobilized target occurs predominantly or exclusively through formation of multivalent bonds between multiple copies of displayed polypeptides on a library member and immobilized target. Accordingly, only members of library displaying multiple copies of a polypeptide are capable of binding to an immobilized target of interest. Conventional libraries typically have a distribution of number of polypeptides per member, in which most members display no copies of a polypeptide, a small proportion display one copy of a polypeptides, a still smaller proportion display two copies, and a still smaller proportion display three or more copies. The methods described in the copending application enrich for the small proportion of conventional display libraries displaying two or more copies of a polypeptide. It is this rare fraction of conventional libraries that is capable of specific binding to an immobilized target.

DEPR:

So efficient are these selection methods that they result in diverse populations in which the vast majority of members retaining full-length coding sequences encode polypeptides having specific affinity for the target of interest, such as the molecular tag. These polypeptides may differ in fine binding specificity within the target and binding affinity for the target. Thus, one can use these methods to identify polypeptides that bind to the target in a manner that is reversible under mild conditions. This procedure involves the use of the target of interest as the affinity reagent. Binding is allowed to proceed to equilibrium and then the target is brought out of solution by contacting with a solid phase

and then the target is brought out of solution by contacting with a solid phase in a process known as panning (Parmley & Smith, Gene 73, 305-318 (1988)). Library members that remain bound to the solid phase do so by virtue of polyvalent bonds between them and target molecules. Unbound library members are washed away from the solid phase. Bound members are then dissociated from the solid phase (e.g., by change of ionic strength or pH). Members that are dissociated under relatively mild conditions such as, for example, a change in ionic strength or pH, or addition of a substance that competes with the tag for binding to the receptor, are then collected and used as capture moieties. For example, binding of metal chelate ligands immobilized on agarose and containing Ni²⁺ to a hexahistidine sequence is easily reversed by adding imidazole to the solution to compete for binding of the metal chelate ligand. Antibody-peptide binding can often be dissociated by raising the pH to 10.5 or higher.

DEPR:

The dissociated library members are now enriched for two features: multivalent display of polypeptides and display of polypeptides having specific affinity for the target of interest. These library members can be subjected to further round(s) of affinity screening to the target without amplification. Alternatively, the library members can be amplified (e.g., by reinfection of bacteria and harvesting of progeny for a phage display library) to produce a secondary library. The secondary library remains enriched for display of polypeptides having specific affinity for the target, but, as a result of amplification, is no longer enriched for polyvalent display of polypeptides. Thus, a second cycle of polyvalent enrichment can then be performed, followed by a second cycle of affinity enrichment to the screening target. Further cycles of affinity enrichment to the screening target, optionally, alternating with amplification and enrichment for polyvalent display can then be performed, until a desired degree of enrichment has been performed.

Full	Title	Citation	Front	Review	Classification	Date	Reference	Claims	KWIC	Draw Desc	Image
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3. Document ID: US 5919665 A

L29: Entry 3 of 5

File: USPT

Jul 6, 1999

DOCUMENT-IDENTIFIER: US 5919665 A

TITLE: Vaccine for clostridium botulinum neurotoxin

DEPR:

The term "monovalent" when used in reference to a clostridial vaccine refers to a vaccine which is capable of provoking an immune response in a host animal directed against a single type of clostridial toxin. For example, if immunization of a host with *C. botulinum* type A toxin vaccine induces antibodies in the immunized host which protect against a challenge with type A toxin but not against challenge with type B, C, D, E, or F toxins, then the type A vaccine is said to be monovalent. In contrast, a "multivalent" vaccine provokes an immune response in a host animal directed against several (i.e., more than one) clostridial toxins. For example, if immunization of a host with a vaccine comprising *C. botulinum* type A and B toxins induces the production of antibodies which protect the host against a challenge with both type A and B toxin, the vaccine is said to be multivalent (in particular, this hypothetical vaccine is bivalent).

DEPR:

The invention contemplates the generation of mono- and multivalent vaccines for the protection of an animal (particularly humans) against several clostridial species. Of particular interest are vaccines which stimulate the production of a humoral immune response to *C. botulinum*, *C. tetani* and *C. difficile* in humans. The antigens comprising the vaccine preparation may be native or recombinantly produced toxin proteins from the clostridial species listed above. When toxin proteins are used as immunogens they are generally modified to reduce the toxicity. This modification may be by chemical or genetic (i.e., recombinant DNA technology) means. In general genetic detoxification (i.e., the expression of nontoxic fragments in a host cell) is preferred as the expression of nontoxic fragments in a host cell precludes the presence of intact, active toxin in the final preparation. However, when chemical modification is desired, the preferred toxin modification is formaldehyde treatment.

DEPR:

The invention contemplates that recombinant *C. botulinum* toxin proteins be used as antigens in mono- and multivalent vaccine preparations. Soluble, substantially endotoxin-free recombinant *C. botulinum* type A toxin proteins may be used alone or in conjunction with either recombinant or native toxins or toxoids from *C. botulinum*, *C. difficile* and *C. tetani* as antigens for the preparation of these mono- and multivalent vaccines. It is contemplated that, due to the structural similarity of *C. botulinum* and *C. tetani* toxin proteins, a vaccine comprising *C. difficile* and botulinum toxin proteins (native or recombinant or a mixture thereof) be used to stimulate an immune response against *C. botulinum*, *C. tetani* and *C. difficile*.

DEPR:

While the different botulinal toxins show structural similarity to one another, the different serotypes are reported to be immunologically distinct (i.e., sera raised against one toxin type does not cross-react to a significant degree with other types). Thus, the generation of multivalent vaccines may require the use of more than one type of toxin. Purification methods have been reported for native toxin types A, B, C, D, E, and F [reviewed in G. Sakaguchi, *Pharmac. Ther.* 19:165 (1983)]. As the different botulinal toxins are structurally related, the invention contemplates the expression of any of the botulinal toxins (e.g., types A-F) as soluble recombinant fusion proteins.

Full	Title	Citation	Front	Review	Classification	Date	Reference	Claims	KWIC	Draw Desc	Image
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4. Document ID: US 5736139 A

L29: Entry 4 of 5

File: USPT

Apr 7, 1998

DOCUMENT-IDENTIFIER: US 5736139 A
TITLE: Treatment of Clostridium difficile induced disease

DEPR:

The term "monovalent" when used in reference to a clostridial vaccine refers to a vaccine which is capable of provoking an immune response in a host (i.e., a subject) animal directed against a single type of clostridial toxin. For example, if immunization of a host with C. difficile type A toxin vaccine induces antibodies in the immunized host which protect against a challenge with type A toxin but not against challenge with type B toxin, then the type A vaccine is said to be monovalent. In contrast, a "multivalent" vaccine provokes an immune response in a host animal directed against several (i.e., more than one) clostridial toxins. For example, if immunization of a host with a vaccine comprising C. difficile type A and B toxins induces the production of antibodies which protect the host against a challenge with both type A and B toxin, the vaccine is said to be multivalent (in particular, this hypothetical vaccine is bivalent).

DEPR:

The invention contemplates the generation of mono- and multivalent vaccines for the protection of an animal (particularly humans) against several clostridial species. Of particular interest are vaccines which stimulate the production of a humoral immune response to C. difficile, C. tetani and C. botulinum in humans. The antigens comprising the vaccine preparation may be native or recombinantly produced toxin proteins from the clostridial species listed above. When toxin proteins are used as immunogens they are generally modified to reduce the toxicity. This modification may be by chemical or genetic (i.e., recombinant DNA technology) means. In general genetic detoxification (i.e., the expression of nontoxic fragments in a host cell) is preferred as the expression of nontoxic fragments in a host cell precludes the presence of intact, active toxin in the final preparation. However, when chemical modification is desired, the preferred toxin modification is formaldehyde treatment.

DEPR:

The invention contemplates that recombinant C. difficile toxin proteins be used as antigens in mono- and multivalent vaccine preparations. Soluble, substantially endotoxin-free recombinant C. difficile toxin A and or toxin B proteins may be used alone or in conjunction with either recombinant or native toxins or toxoids from C. botulinum, C. difficile and C. tetani as antigens for the preparation of these mono- and multivalent vaccines. It is contemplated that, due to the structural similarity of C. botulinum and C. tetani toxin proteins, a vaccine comprising C. difficile and botulinum toxin proteins (native or recombinant or a mixture thereof) be used to stimulate an immune response against C. botulinum, C. tetani and C. difficile.

Full	Title	Citation	Front	Review	Classification	Date	Reference	Claims	KWIC	Draw Desc	Image
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5. Document ID: US 4292307 A

L29: Entry 5 of 5

File: USPT

Sep 29, 1981

DOCUMENT-IDENTIFIER: US 4292307 A

TITLE: Vaccine and method for prophylaxis and treatment of clostridiosis of animals and poultry

BSPR:

A a polyvalent antigenic vaccine against clostridiosis of animals, is known comprising antigens that are anacultures of Cl. perfringens types B, C, and D, Cl. oedematiens, Cl. septicum, Cl. tetani, and Cl. chauvoei, a mineral oil, a nonionic lipophilic emulsifying agent, and a nonionic hydrophilic emulsifying agent.

BSPR:

The proposed vaccine possesses high antigenic and immunogenic properties and produces in vaccinated animals an effective antitoxic immunity to all said causative agents. The immunity persists from 1 to 2 years. The immunity to specific agents can last to 5 years. The vaccine dose is reduced two times. The titers of antitoxins in animals toward all monotoxoids increase 8-10 times, and the antitoxins are produced twice as fast. Following the primary immunization, the animals are re-vaccinated only once in their lifetime or only for special epizootic indications (at intervals from 2 to 5 years). The intensity of the immunity is 15-20 times higher than that attained with the known polyvalent toxoid-vaccine. The preparation is harmless and areactogenic for both vaccinated animals and man (milk and meat of vaccinated animals). The time of expiration of the vaccine has increased to five years.

Full	Title	Citation	Front	Review	Classification	Date	Reference	Claims	KWIC	Draw Desc	Image
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Terms	Documents
122 and 127	5

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Documents, starting with Document:

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Display Format: KWIC

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WEST **Generate Collection**

L32: Entry 18 of 97

File: USPT

Apr 18, 2000

DOCUMENT-IDENTIFIER: US 6051239 A

TITLE: Compositions and methods for systemic delivery of oral vaccines and therapeutic agents

BSPR:

The present invention relates to compositions and methods for systemic delivery of orally administered vaccines and therapeutic agents via a modified botulinum toxin, wherein said toxin maintains its ability to translocate across the gut wall but has been altered to be non-toxic.

BSPR:

Clostridial neurotoxins are the most potent protein toxins known. The neurotoxin produced from *Clostridium tetani* (tetanus toxin) is encountered by humans as a result of open wounds. However, tetanus poisoning at least in industrial countries is no longer a major public health problem due to the availability and widespread use of a safe, effective and inexpensive vaccine. This vaccine is basically a formalin-inactivated culture supernatant from *C. tetani* grown in fermentors.

BSPR:

Botulinum neurotoxin (BoNT), which is produced by the organisms *Clostridium botulinum*, *Clostridium butyricum* and *Clostridium baratii*, is the potent etiologic agent associated with the disease botulism (Simpson, L. Annu. Rev. Pharmacol. Toxicol. 1986 26:427-453). Humans are usually exposed to this neurotoxin through food poisoning, although there are rare incidents of wound botulism. A similar vaccine to the tetanus vaccine has been developed to provide protection from botulinum toxin poisoning. However, since there are seven different serotypes of botulinum toxin, complete protection with this inactivated toxin can be afforded only by making seven distinct vaccines and combining them for administration. Presently, only five of the seven serotypes are represented in the botulinum toxin vaccine. Further, some of the serotypes are composed of strains that do not produce high levels of toxin in culture. Thus, growth, purification and inactivation of the toxins for vaccine purposes is time consuming and expensive, owing to the high hazards associated with handling fully active toxin (Clayton et al. Infection and Immunity 1995 63(7):2738-2742). At this time this vaccine is only available through the Center of Disease Control for primarily experimental use.

BSPR:

The heavy chain of the toxin is believed to be essential for binding and translocation of the toxin from the outside to the inside of the cholinergic nerve endings, while the light chain possesses the zinc-dependent endoprotease activity that accounts for the ability of the toxin to poison cholinergic nerve endings (Neimann et al. Behring Inst. Mitt. 1991 89:153-162). Accordingly, vaccines against botulism comprising a nontoxic 50 kDa carboxyterminal fragment of *Clostridium botulinum* have been described. LaPenotiere et al. Toxicon 1995 33(10):1383-6 and Clayton et al. Infection and Immunity 1995 63(7):2738-2742. Further, it has been suggested that this highly selective neurotoxin and tetanus toxin may be converted into nontoxic therapeutic tools that can be applied in delivery of drugs, hormones, enzymes or antiviral substances to the central nervous system.

BSPR:

An object of the present invention is to provide a modified botulinum toxin which maintains its ability to translocate from the gut into the general circulation but which is nontoxic. The modified botulinum toxin can be used as an oral

vaccine for antigenic peptides including botulinum toxin and for the oral delivery of other therapeutic agents to the general circulation.

DEPR:

Accordingly, results from these experiments demonstrate that a modified botulinum toxin can be constructed in accordance with the teachings provided herein that is nontoxic but which retains the ability to translocate from the gut to the general circulation and to evoke protective antibodies. Further, compositions comprising a modified botulinum toxin of the present invention are clearly effective as oral vaccines against botulism in animals.

DEPR:

In addition, because the modified botulinum toxins of the present invention retain their ability to translocate from the gut and to be delivered intact to the general circulation, these modified botulinum toxins can be used as delivery vehicles for oral administration of antigens to proteins other than botulinum toxin and therapeutic agents to the general circulation. There are various ways in which the modified botulinum toxin could be used as a carrier for oral vaccines. For example, because the inactivation of the zinc binding motif of the light chain does not adversely affect the toxin's ability to translocate out of the gut, the zinc binding motif of the native botulinum toxin can be replaced with a selected antigen for a different protein, i.e. a protein other than botulism, to produce an oral vaccine against this different protein. Alternatively, well known techniques of protein chemistry and molecular biology can be used to attach the selected antigen or a portion thereof to a modified botulinum toxin. The resulting modified botulinum toxin would not only be nontoxic, but also retain its ability to translocate from the gut to the general circulation so that the selected antigen, when administered orally, would reach the general circulation to evoke a systemic immune response against the protein. Examples of vaccines which could be administered orally with the modified botulinum toxin include, but are not limited to, vaccines for Bacille Calmette-Guerin, cholera, diphtheria, hepatitis B, measles, meningitis, mumps, pertussis, plague, polio, rabies, rubella, tetanus, typhoid, and yellow fever. The oral vaccine can be administered individually or in combination, such as for DTP (diphtheria, tetanus, pertussis). The ability to deliver an oral vaccine is especially important for areas in which medical personnel are not readily available. Moreover, an oral vaccine of the present invention would represent an important economic advantage in addition to diminishing the need for skilled personnel as it would eliminate costs associated with syringes used for injection and/or for the disposal of used syringes.

DEPR:

Formulations of oral vaccines of the present invention preferably comprise the modified botulinum toxin in a pharmacologically acceptable carrier, such as sterile physiological saline, sterile saline with 0.1% gelatin, or sterile saline with 1.0 mg/ml bovine serum albumin. Alternatively, the modified botulinum toxin of the present invention can be genetically engineered into a plant so that food produced by the plant such as a potato or a banana can serve as a vector for widescale vaccination. Methods of genetically engineering plants to express a foreign peptide are well known in the art as exemplified by PCT/US96/09558, filed Jun. 6, 1996.

DEPR:

The general concepts for use of a modified botulinum toxin as a carrier for vaccines or other therapeutic agents are the same for human and for non-human animals, with one exception. All serotypes of botulinum toxin are not likely to be equally efficacious as carriers for drugs in all species. Clinical evidence suggests that humans are especially sensitive to the effects of serotypes A, B, and E. This may relate to the efficiency with which these three serotypes are absorbed from the gastrointestinal system. Thus, serotypes A, B, and E would be preferred carriers of therapeutic agents for humans.

DEPR:

On the contrary, most non-human animals are particularly sensitive to serotype C. This suggests that as to veterinary medicine, the preferred carrier of therapeutic agents for non-human animal use would be serotype C. Examples of animal vaccines which could be administered orally with the modified botulinum toxin include, but are not limited to, ones for adenovirus type 2, Bordetella bronchiseptica, botulism, calicivirus, Chlamydia psittaci, clostridial diseases,

such as *Clostridium Perfringens* type C, coronaviruses, distemper, equine encephalomyelitis, *Escherichia coli*, feline infectious peritonitis, feline leukemia virus, feline panleukopenia, hepatitis, leptospirosis, parainfluenza virus, parvoviruses, rabies, rhinotracheitis virus, and tetanus.

ORPL:

Clayton et al., "Protective Vaccination with a Recombinant Fragment of *Clostridium botulinum* Neurotoxin Serotype A Expressed from a Synthetic Gene in *Escherichia coli*," *Infection and Immunity* 1995 63(7):2738-2742.

WEST **Generate Collection**

L32: Entry 21 of 97

File: USPT

Dec 7, 1999

DOCUMENT-IDENTIFIER: US 5997856 A

TITLE: Method and compositions for solubilization and stabilization of polypeptides, especially proteins

DEPR:

Other polypeptides contemplated by this invention are polypeptides specifically intended for veterinary use, including vaccines, animal growth factors and bovine interferons and interleukin-2. Illustrative vaccines include: bovine vaccines, for example those for anthrax, clostridium (multiple species), pasteurella, leptospira pomona, bovine diarrhea, brucellosis, parainfluenza, 3-respiratory syncytial virus, tetanus, vesicular stomatitis and staphylococcus; canine vaccines, for example those for bordetella, coronavirus, distemper, parvovirus, parainfluenza and rabies; equine vaccines, for example those for anthrax, encephalomyelitis, influenza, tetanus, rabies and streptococcus-strangles; feline vaccines, such as those for leukemia, pneumonitis-chlamydia and rabies; ovine vaccines, for example those for anthrax, blackleg, bluetongue, enterotoxemia, tetanus and vibriosis; and porcine vaccines, for example those for anthrax, enterotoxemia, dysentery, erysipelas, leptospirosis, parvovirus, pseudorabies, tetanus and rotavirus.

WESTGenerate Collection

L32: Entry 41 of 97

File: USPT

Sep 29, 1998

DOCUMENT-IDENTIFIER: US 5814338 A

TITLE: Drug delivery system

DEPR:

Other polypeptides contemplated by this invention are polypeptides specifically intended for veterinary use, including vaccines, animal growth factors and bovine interferons and interleukin-2. Illustrative vaccines include: bovine vaccines (for example those for anthrax, clostridium (multiple species), pasteurelia, leptospira pomona, bovine diarrhoea, brucellosis, parainfluenza, 3-respiratory syncytial virus, tetanus, vesicular stomatitis and staphylococcus), canine vaccines (for example those for bordetella, coronavirus, distemper, parvovirus, parainfluenza and rabies), equine vaccines (for example those for anthrax, encephalomyelitis, influenza, tetanus, rabies and streptococcus-strangles), feline vaccines (such as those for leukemia, pneumonitis-chlamydia and rabies), ovine vaccines (for example those for anthrax, blackleg, bluetongue, enterotoxemia, tetanus and vibriosis) and porcine vaccines (for example those for anthrax, enterotoxemia, dysentery, erysipelas, leptospirosis, parvovirus, pseudorabies, tetanus and rotavirus).

WEST **Generate Collection**

L32: Entry 45 of 97

File: USPT

Apr 7, 1998

DOCUMENT-IDENTIFIER: US 5736139 A

TITLE: Treatment of Clostridium difficile induced disease

BSPR:

The present invention relates to clostridial antitoxin and vaccine therapy for humans and other animals. Antitoxins which neutralize the pathologic effects of clostridial toxins are provided. Vaccines which prevent the morbidity and mortality associated with clostridial diseases are provided.

BSPR:

Immunization of subjects with toxin preparations has been done in an attempt to induce immunity against botulinum toxins. A C. botulinum vaccine comprising chemically inactivated (i.e., formaldehyde-treated) type A, B, C, D and E toxin is commercially available for human usage. However, this vaccine preparation has several disadvantages. First, the efficacy of this vaccine is variable (in particular, only 78% of recipients produce protective levels of anti-type B antibodies following administration of the primary series). Second, immunization is painful (deep subcutaneous inoculation is required for administration), with adverse reactions being common (moderate to severe local reactions occur in approximately 6% of recipients upon initial injection; this number rises to approximately 11% of individuals who receive booster injections) [Informational Brochure for the Pentavalent (ABCDE) Botulinum Toxoid, Centers for Disease Control]. Third, preparation of the vaccine is dangerous as active toxin must be handled by laboratory workers.

BSPR:

What is needed are safe and effective vaccine preparations for administration to those at risk of exposure to C. botulinum toxins.

DEPR:

The term "therapeutic vaccine" when used in reference to a vaccine comprising one or more recombinant clostridial toxin fusion proteins means that the vaccine contains an immunologically-effective amount of the fusion proteins (i.e., the immunogens).

DEPR:

The term "monovalent" when used in reference to a clostridial vaccine refers to a vaccine which is capable of provoking an immune response in a host (i.e., a subject) animal directed against a single type of clostridial toxin. For example, if immunization of a host with C. difficile type A toxin vaccine induces antibodies in the immunized host which protect against a challenge with type A toxin but not against challenge with type B toxin, then the type A vaccine is said to be monovalent. In contrast, a "multivalent" vaccine provokes an immune response in a host animal directed against several (i.e., more than one) clostridial toxins. For example, if immunization of a host with a vaccine comprising C. difficile type A and B toxins induces the production of antibodies which protect the host against a challenge with both type A and B toxin, the vaccine is said to be multivalent (in particular, this hypothetical vaccine is bivalent).

DEPR:

The invention further contemplates a method of vaccinating a subject to produce neutralizing antitoxin directed against C. difficile toxin comprising: a) providing in any order: i) a subject, ii) a first purified soluble and substantially endotoxin-free protein comprising a portion of Clostridium difficile toxin A sequence SEQ ID NO:6, and iii) a second purified soluble and

substantially endotoxin-free protein comprising a portion of Clostridium difficile toxin B sequence SEQ ID NO:10; B) mixing the first and second proteins to create a therapeutic vaccine; and c) vaccinating the subject with the therapeutic vaccine so as to generate neutralizing antitoxin. The method of vaccination is not limited by the nature or species of the subject. In one embodiment the subject is a bird. In another embodiment the subject is a mammal. In yet another embodiment the subject is a human. In a still further embodiment, the method of vaccination the first and second toxin proteins further comprise at least one non-toxin protein sequence. The invention is not limited by the nature of the non-toxin protein sequence. In one embodiment, the non-toxin protein sequence comprises a poly-histidine tract. In another embodiment, the non-toxin protein sequence comprises the maltose binding protein. In yet another embodiment, the non-toxin protein sequence comprises a thioredoxin protein.

DEPR:

The present invention contemplates vaccinating humans and other animals polypeptides derived from C. botulinum neurotoxin which are substantially endotoxin-free. These botulin peptides are also useful for the production of antitoxin. Anti-botulin toxin antitoxin is useful for the treatment of patients effected by or at risk of symptoms due to the action of C. botulinum toxins. The organisms, toxins and individual steps of the present invention are described separately below.

DEPR:

V. Vaccines Against Clostridial Species

DEPR:

The invention contemplates the generation of mono- and multivalent vaccines for the protection of an animal (particularly humans) against several clostridial species. Of particular interest are vaccines which stimulate the production of a humoral immune response to C. difficile, C. tetani and C. botulinum in humans. The antigens comprising the vaccine preparation may be native or recombinantly produced toxin proteins from the clostridial species listed above. When toxin proteins are used as immunogens they are generally modified to reduce the toxicity. This modification may be by chemical or genetic (i.e., recombinant DNA technology) means. In general genetic detoxification (i.e., the expression of nontoxic fragments in a host cell) is preferred as the expression of nontoxic fragments in a host cell precludes the presence of intact, active toxin in the final preparation. However, when chemical modification is desired, the preferred toxin modification is formaldehyde treatment.

DEPR:

The invention contemplates that recombinant C. difficile toxin proteins be used as antigens in mono- and multivalent vaccine preparations. Soluble, substantially endotoxin-free recombinant C. difficile toxin A and or toxin B proteins may be used alone or in conjunction with either recombinant or native toxins or toxoids from C. botulinum, C. difficile and C. tetani as antigens for the preparation of these mono- and multivalent vaccines. It is contemplated that, due to the structural similarity of C. botulinum and C. tetani toxin proteins, a vaccine comprising C. difficile and botulinum toxin proteins (native or recombinant or a mixture thereof) be used to stimulate an immune response against C. botulinum, C. tetani and C. difficile.

DEPR:

When recombinant clostridial toxin proteins produced in gram-negative bacteria (e.g., E. coli) are used as vaccines, they are purified to remove endotoxin prior to administration to a host animal. In order to vaccinate a host, an immunogenically-effective amount of purified substantially endotoxin-free recombinant clostridial toxin protein is administered in any of a number of physiologically acceptable carriers known to the art. When administered for the purpose of vaccination, the purified substantially endotoxin-free recombinant clostridial toxin protein may be used alone or in conjunction with known adjuvants, including potassium alum, aluminum phosphate, aluminum hydroxide, Gerbu adjuvant (GMDP; C.C. Biotech Corp.), RIBI adjuvant (MPL; RIBI Immunochemical Research, Inc.), QS21 (Cambridge Biotech). The alum and aluminum-based adjuvants are particularly preferred when vaccines are to be administered to humans. The route of immunization may be nasal, oral, intramuscular, intraperitoneal or subcutaneous.

DEPR:

Example 23 demonstrated that neutralizing antibodies are generated by immunization with the pMBot protein expressed in *E. coli*. These results showed that the pMBot fusion protein is a good vaccine candidate. However, immunogens suitable for use as vaccines should be pyrogen-free in addition to having the capability of inducing neutralizing antibodies. Expression clones and conditions that facilitate the production of *C. botulinum* C fragment protein for utilization as a vaccine were developed.

ORPL:

Lyerly, D.M., et al., "Vaccination Against Lethal *Clostridium difficile* Enterocolitis with a Nontoxic Recombinant Peptide of Toxin A," *Curr. Microbiol.* 21:29 (1990).

ORPL:

H.F. LaPenotiere, et al., "Development of a Molecular Engineered Vaccine for *C. botulinum* Neurotoxins," in *Botulinum and Tetanus Neurotoxins*, B.R. DasGupta, ed., Plenum Press, New York, pp. 463-466, (1993).

WEST

Generate Collection

L32: Entry 46 of 97

File: USPT

Mar 24, 1998

US-PAT-NO: 5730969

DOCUMENT-IDENTIFIER: US 5730969 A

TITLE: Method and compositions for solubilization and stabilization of polypeptides, especially proteins

DATE-ISSUED: March 24, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Hora; Maninder Singh	Rodeo	CA	N/A	N/A
Rubinfeld; Joseph	Danville	CA	N/A	N/A
Stern; Warren	Gainesville	FL	N/A	N/A
Wong; Gregory J.	San Leandro	CA	N/A	N/A

ASSIGNEE-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY	TYPE CODE
Chiron Corporation	Emeryville	CA	N/A	N/A	02

APPL-NO: 8/ 474178

DATE FILED: June 7, 1995

PARENT-CASE:

CROSS-REFERENCE TO RELATED APPLICATION This application is a divisional of application Ser. No. 07/373,928, filed Jun. 29, 1989, which is a continuation-in-part of applicants' application Ser. No. 07/253,720, filed Oct. 5, 1988, now abandoned, incorporated by reference herein in its entirety and relied upon.

INT-CL: [6] A61K 38/17, A61K 38/19, A61K 38/20, A61K 38/49

US-CL-ISSUED: 424/85.1; 424/85.2, 424/85.4, 424/85.6, 424/94.3, 514/2, 514/3, 514/12, 514/21

US-CL-CURRENT: 424/85.1; 424/85.2, 424/85.4, 424/85.6, 424/94.3, 514/12, 514/2, 514/21, 514/3

FIELD-OF-SEARCH: 435/188, 424/85.1, 424/85.2, 424/85.4, 424/85.5, 424/85.6, 424/85.7, 424/94.3, 530/303, 530/351, 530/399, 514/2, 514/3, 514/12, 514/21

PRIOR-ART-DISCLOSED:

U.S. PATENT DOCUMENTS

Search Selected

Search ALL

PAT-NO	ISSUE-DATE	PATENTEE-NAME	US-CL
<u>3459731</u>	August 1969	Gramera et al.	260/209
<u>4024223</u>	May 1977	Noda et al.	424/180
<u>4228160</u>	October 1980	Szejtli et al.	424/180
<u>4232009</u>	November 1980	Hayashi et al.	424/180
<u>4351846</u>	September 1982	Matsumoto et al.	424/305

<u>4352793</u>	October 1982	Yamahira et al.	424/180
<u>4383992</u>	May 1983	Lipari	424/238
<u>4407795</u>	October 1983	Nicolau et al.	424/180
<u>4424209</u>	January 1984	Tuttle	424/180
<u>4425336</u>	January 1984	Tuttle	424/180
<u>4438106</u>	March 1984	Wagu et al.	424/180
<u>4457916</u>	July 1984	Hayashi et al.	424/101
<u>4474811</u>	October 1984	Masuda et al.	424/317
<u>4478995</u>	October 1984	Shinoda et al.	536/46
<u>4479944</u>	October 1984	Hayashi et al.	424/180
<u>4479966</u>	October 1984	Hayashi et al.	424/305
<u>4497803</u>	February 1985	Harada et al.	514/450
<u>4499085</u>	February 1985	Masuda	514/58
<u>4505893</u>	March 1985	Mori et al.	424/94
<u>4518588</u>	May 1985	Szejtli et al.	514/58
<u>4524068</u>	June 1985	Szejtli et al.	514/58
<u>4552760</u>	November 1985	Murakami et al.	424/94
<u>4555504</u>	November 1985	Jones	514/26
<u>4565807</u>	January 1986	Uekama et al.	514/58
<u>4568544</u>	February 1986	Hasegawa et al.	424/94
<u>4575548</u>	March 1986	Ueda et al.	536/46
<u>4596795</u>	June 1986	Pitha	514/58
<u>4598070</u>	July 1986	Ohwaki et al.	514/58
<u>4603123</u>	July 1986	Chiesi et al.	514/58
<u>4608366</u>	August 1986	Hasegawa et al.	514/58
<u>4623641</u>	November 1986	Szejtli et al.	514/58
<u>4659696</u>	April 1987	Hirai et al.	514/15
<u>4663316</u>	May 1987	Ninger et al.	519/99
<u>4675395</u>	June 1987	Fukazawa et al.	536/103
<u>4727064</u>	February 1988	Pitha	514/58
<u>4728509</u>	March 1988	Shimizu et al.	424/81
<u>4728510</u>	March 1988	Shibanai et al.	424/94.5
<u>4751095</u>	June 1988	Karl et al.	426/548
<u>4764604</u>	August 1988	Muller	536/103
<u>4897472</u>	January 1990	Korpela et al.	536/46
<u>4925678</u>	May 1990	Ranney	424/493
<u>4983586</u>	January 1991	Bodor	514/58
<u>5002935</u>	March 1991	Bodor	514/58

<u>1</u>	<u>5120720</u>	June 1992	Pitha et al.	514/58
<u>1</u>	<u>5580856</u>	December 1996	Prestrelski et al.	514/21

FOREIGN PATENT DOCUMENTS

FOREIGN-PAT-NO	PUBN-DATE	COUNTRY	US-CL
1222697	June 1987	CAX	
3094157	November 1983	EPX	
5123291	October 1984	EPX	
5133767	March 1985	EPX	
5149197	July 1985	EPX	
5231132	August 1987	EPX	
5335545	October 1989	EPX	
62-164701	July 1978	JPX	
59/104556	June 1984	JPX	
61/070996	April 1986	JPX	
61/197602	September 1986	JPX	
61/236802	October 1986	JPX	
61/287901	December 1986	JPX	
61/287902	December 1986	JPX	
62-106901	May 1987	JPX	
62/223129	October 1987	JPX	
62/281855	December 1987	JPX	
63/036793	February 1988	JPX	
63/027440	February 1988	JPX	
63/135402	June 1988	JPX	
85/02767	July 1985	WOX	

OTHER PUBLICATIONS

Molecular Pharmacology, vol. 32, Issued Jul. 1987, Laurenza et al, "Stimulation of Adenylate Cyclase . . . ", pp. 133-139.
Hagenlocher and Pearlman, Pharm. Res. 6:S30 (1989).
Loftsson et al, Eur. J. Pharm. Sci. 1:95 (1993).
Pitha and Hoshino, Int. J. Pharm. 80:243 (1992).
Kraus et al, Pharm. Ztg. Wiss. 136/4:11 (1991).
Manning et al, Pharm. Res. 6:903 (1989).
Johnson et al, J. Pharm. Sci. 83:1142 (1994).
Brewster et al, Int. J. Pharm. 75:R5 (1991).
Brewster et al, J. Parent. Sci. Technol. 43:231 (1989).
Brewster et al, J. Pharm. Sci. 77:981 (1988).
Uekama, 1987, Topics in Pharmaceutical Sciences, 181-194.
Okada et al., 1988, Chem. Pharm. Bull. 36:2176-2185.
Kyoka et al., 1987, Chem. Pharm. Bull. 35:3413-3418.
Yamamoto et al., 1989, Intl. Journal of Pharmaceutics 49:163-171.
Wang et al., 1988, Parenteral Formulations of Proteins and Peptides: Stability and Stabilizers 42:2S-S26.
Uekama, Mar., 1985, Pharmacy International, 61-65.
Pitha, 1984, J. Inclusion Phenomena 2:477-485.
Fenyvesi, 1984, Chem. Pharm. Bull. 32(2):665-669.
Uekama et al., 1985, International Journal of Pharmaceutics 23:35-42.
Pitha et al., 1985, J. Pharmaceutical Sciences 74(9):987-990.
Pitha et al., 1986, International J. Pharmaceutics 29:73-82.
Uekama et al., 1987, CRC Critical Reviews in Therapeutic Drug Carrier Systems 3(1):1-40.
Okada et al., 1988, Chem. Pharm. Bull. 36(6):2176-2185.
Matsuyama et al., 1987, Drug Development and Industrial Pharmacy 13(15):2687-2691.
Grant and Hackh's Chemical Dictionary, fifth edition, 431(1987).

Brewster et al., Pharmaceutical Res., vol. 8, No. 6, 792-795 (1991).
Derwent Chemical Patent Index/Documentation Abstracts Journal, Week 7948, 86688B (1979), abstract of JP 54/135215, published Oct. 1979.
Chem. Abstracts, vol. 99, 500, 120601n (1983), abstract of JP 58/092691 published Jun. 1983.
Derwent Chemical Patent Index/Documentation Abstracts Journal, Week 8528, 169436 (1985), abstract of JP 60/100524, published Jun. 1985.
Derwent Chemical Patent Index/Documentation Abstracts Journal, Week 8545, 279148 (1985), abstract of JP 60/188067, published Sep. 1985.
Derwent Chemical Patent Index/Documentation Abstracts Journal, Week 8632, 207158 (1986), abstract of JP 61/137827, published Jun. 1986.
Chemical Abstracts, vol. 110, No. 14, abstract No. 121420k, abstract of JP 63/115821 (1989).

ART-UNIT: 181

PRIMARY-EXAMINER: Russel; Jeffrey E.

ATTY-AGENT-FIRM: Burns, Doane, Swecker & Mathis, L.L.P.

ABSTRACT:

The invention provides a method for the solubilization and/or stabilization of polypeptides, especially proteins, using a cyclodextrin selected from the group consisting of hydroxypropyl, hydroxyethyl, glucosyl, maltosyl and maltotriosyl derivatives of .beta.- and .gamma.-cyclodextrin. Solubilized and/or stabilized compositions comprising a polypeptide, especially a protein, and the selected cyclodextrin are also described.

79 Claims, 4 Drawing figures

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L32: Entry 46 of 97

File: USPT

Mar 24, 1998

DOCUMENT-IDENTIFIER: US 5730969 A

TITLE: Method and compositions for solubilization and stabilization of polypeptides, especially proteins

DEPR:

Other polypeptides contemplated by this invention are polypeptides specifically intended for veterinary use, including vaccines, animal growth factors and bovine interferons and interleukin-2. Illustrative vaccines include: bovine vaccines, for example those for anthrax, clostridium (multiple species), pasteurella, leptospira pomona, bovine diarrhea, brucellosis, parainfluenza, 3-respiratory syncytial virus, tetanus, vesicular stomatitis and staphylococcus; canine vaccines, for example those for bordetella, coronavirus, distemper, parvovirus, parainfluenza and rabies; equine vaccines, for example those for anthrax, encephalomyelitis, influenza, tetanus, rabies and streptococcus-strangles; feline vaccines, such as those for leukemia, pneumonitis-chlamydia and rabies; ovine vaccines, for example those for anthrax, blackleg, bluetongue, enterotoxemia, tetanus and vibriosis; and porcine vaccines, for example those for anthrax, enterotoxemia, dysentery, erysipelas, leptospirosis, parvovirus, pseudorabies, tetanus and rotavirus.

WEST**Generate Collection****Search Results - Record(s) 1 through 6 of 6 returned.****1. Document ID: US 6051239 A**

L34: Entry 1 of 6

File: USPT

Apr 18, 2000

US-PAT-NO: 6051239

DOCUMENT-IDENTIFIER: US 6051239 A

TITLE: Compositions and methods for systemic delivery of oral vaccines and therapeutic agents

Full	Title	Citation	Front	Review	Classification	Date	Reference	Claims	KWIC	Draw Desc	Image
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2. Document ID: US 5814338 A

L34: Entry 2 of 6

File: USPT

Sep 29, 1998

US-PAT-NO: 5814338

DOCUMENT-IDENTIFIER: US 5814338 A

TITLE: Drug delivery system

Full	Title	Citation	Front	Review	Classification	Date	Reference	Claims	KWIC	Draw Desc	Image
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3. Document ID: US 5725853 A

L34: Entry 3 of 6

File: USPT

Mar 10, 1998

US-PAT-NO: 5725853

DOCUMENT-IDENTIFIER: US 5725853 A

TITLE: 4 strain direct-fed microbial

Full	Title	Citation	Front	Review	Classification	Date	Reference	Claims	KWIC	Draw Desc	Image
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4. Document ID: US 5283172 A

L34: Entry 4 of 6

File: USPT

Feb 1, 1994

US-PAT-NO: 5283172

DOCUMENT-IDENTIFIER: US 5283172 A

TITLE: Type-C rotavirus cultures and uses therefor

Full	Title	Citation	Front	Review	Classification	Date	Reference	Claims	KWIC	Draw Desc	Image
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5. Document ID: US 5219578 A

L34: Entry 5 of 6

File: USPT

Jun 15, 1993

US-PAT-NO: 5219578

DOCUMENT-IDENTIFIER: US 5219578 A

TITLE: Composition and method for immunostimulation in mammals

Full	Title	Citation	Front	Review	Classification	Date	Reference	Claims	KWOC	Draw Desc	Image
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6. Document ID: US 4292307 A

L34: Entry 6 of 6

File: USPT

Sep 29, 1981

US-PAT-NO: 4292307

DOCUMENT-IDENTIFIER: US 4292307 A

TITLE: Vaccine and method for prophylaxis and treatment of clostridiosis of animals and poultry

Full	Title	Citation	Front	Review	Classification	Date	Reference	Claims	KWOC	Draw Desc	Image
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Terms	Documents
('5725853' '6051239' '5814338' '5283172' '5219578' '4292307')[PN]	6

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Documents, starting with Document: 6

Display Format: TI

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L32: Entry 93 of 97

File: USPT

Oct 9, 1979

DOCUMENT-IDENTIFIER: US 4170645 A

TITLE: Antibacterial agent BM123.gamma., salts and alkyl derivatives thereof for the control of shipping fever in cattle

DEPR:

Calves weighing 90.6 to 181.2 Kg received at the feedlot are processed as is normally done, except no antibacterial treatment is given. Processing includes vaccination with Infectious Bovine Rhinotracheitis (Bovine virus Diarrhea) Leptospirosis vaccine, administration of a Clostridium novyi, septicum, sordelli, chauvei bacterin, levamisole (1/2 oblet), i.m. administration of 3 ml of a vitamin A, D and E formulation, a pour-on formulation of 0,0-dimethyl-0-(2,4,5-trichlorophenyl) ester of phosphorothioic acid for the control of grubs and lice, and one DES (diethylstilbestrol) implant in an ear. In addition--and at the same time--the calves are branded, ear tagged, dehorned and castrated where applicable.

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Database: IBM Technical Disclosure Bulletins

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(wovyi or perfringens or tetani or
tertium or bifermentans or botulinum or
sporogenes or haemolyticum or chauvoei

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Search History

Today's Date: 4/5/2001

<u>DB Name</u>	<u>Query</u>	<u>Hit Count</u>	<u>Set Name</u>
USPT	(wovyi or perfringens or tetani or tertium or bifermentans or botulinum or sporogenes or haemolyticum or chauvoei or specticum or novyi or sordellii or clostrid\$) near50 vaccin\$	97	L32
USPT	l27 and (virus or viruses or viral or respiratory)	24	L31
USPT	l29 and (virus or viruses or viral or influenza)	1	L30
USPT	l22 and l27	5	L29
USPT	l27 and (l15 or l16 or l9)	3	L28
USPT	(wovyi or perfringens or tetani or tertium or bifermentans or botulinum or sporogenes or haemolyticum or chauvoei or specticum or novyi or sordellii or clostrid\$) .ti.	81	L27
USPT	l25 and (wovyi or perfringens or tetani or tertium or bifermentans or botulinum or sporogenes or haemolyticum or chauvoei or specticum or novyi or sordellii)	19	L26
USPT	l22.clm.	6112	L25

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L14: Entry 10 of 29

File: USPT

Mar 9, 1999

DOCUMENT-IDENTIFIER: US 5879685 A

TITLE: Immunostimulating and immunopotentiating reconstituted influenza virosomes and vaccines containing them

BSPR:

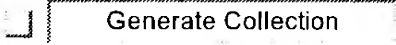
Surface-active agents such as saponin or Quil A.backslash. in immunostimulating complexes (iscoms) have been used in a number of experimental and veterinary vaccines. They improved the immunogenicity of several antigens, especially of viral membrane proteins.

CLPR:

9. An IRIV of claim 5 wherein the bacteria is Clostridium tetani.

CLPR:

20. An IRIV of claim 15 wherein the bacteria is Clostridium tetani.

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L14: Entry 16 of 29

File: USPT

Jan 14, 1997

DOCUMENT-IDENTIFIER: US 5593697 A
TITLE: Single dose vaccination system

BSPR:

International Patent Application No. WO 91/04052 describes a solid vaccine composition containing an antigenic substance, saponin, and a polycationic adjuvant, which may be formulated as an implant in which pulsed release may be achieved by coating the vaccine with different thicknesses of polymer.

DEPR:

Apart from the ingredients already listed, the implants of the invention may be formulated with conventional additives known per se in the tableting art, especially lubricating agents, such as magnesium stearate. Additives which enhance the immune response may also be added. These are loosely termed adjuvants, examples of which include but are not limited to aluminium salts, calcium phosphate, saponin, Quil A, dextran sulphate, DEAE dextran, muramyl dipeptide, DDA (dimethyl dioctadecyl ammonium bromide), Montanide 451, LPS (lipopolysaccharide) and various bacterial wall extracts.

CLPR:

11. An implant according to claim 9 or claim 10 wherein the antigen is selected from the group consisting of caseous lymphadenitis toxoid, Clostridium botulinum toxoid, tetanus toxoid, and luteinizing hormone releasing hormone.

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L20: Entry 25 of 64

File: USPT

Jan 5, 1999

DOCUMENT-IDENTIFIER: US 5855894 A

TITLE: Pasteurella haemolytica type A-1 bacterin-toxoid vaccine

DEPR:

Still other preferred vaccine compositions of this invention result from combining the vaccine of this invention with other vaccinal agents, particularly antigens of other BRDC pathogens. An illustrative example is a vaccine composition formed by the combination of antigens from Pasteurella multocida, Haemophilus somnus, Clostridial species, Mycoplasma species, Bovine Respiratory Syncytial Virus, Bovine Viral Diarrhea Virus, Bovine Parainfluenza Type 3 virus.

DEPR:

Vaccines of the invention may be prepared as pharmaceutical compositions containing a therapeutically effective amount of the supernatant as the active ingredient in a nontoxic and sterile pharmaceutically acceptable carrier. A preferred embodiment of the vaccine of the invention is where the vaccine is in freeze-dried form and reconstituted with at least one adjuvant just prior to use. Such a vaccine is preferred as it provides increased stability and reduced free endotoxin, which reduces post-vaccinal systemic reactions. Such adjuvants include, among others, a mineral oil and lecithin emulsion ["AMPHIGEN" mineral oil/lecithin emulsion, Hydronics, Inc.] as taught in U.S. Pat. No. 5,084,269 or other dispersed oils, aluminum hydroxide, muramyl dipeptide, and saponins, such as Quil A. The disclosure of U.S. Pat. No. 5,084,269 is incorporated by reference as if fully set forth herein.

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L20: Entry 43 of 64

File: USPT

Oct 15, 1996

DOCUMENT-IDENTIFIER: US 5565203 A

TITLE: Hepatitis A virus in a reconstituted influenza virosome and use as a vaccine

BSPR:

Surface-active agents such as saponin or Quil A .backslash. in immunostimulating complexes (iscoms) have been used in a number of experimental and veterinary vaccines. They improved the immunogenicity of several antigens, especially of viral membrane proteins.

BSPR:

In a preferred embodiment, the present invention relates to IRIVs wherein said antigen is derived from a pathogen including parts thereof. Preferred examples of such pathogens are a virus, a bacterium, a parasite, anti-idiotypic (Anti-Id) antibodies mimicking said viruses, bacteria or parasites, antibodies against said viruses, bacteria or parasites, or a toxin. Examples of viruses are hepatitis A, B, C, D or E virus, Polio virus, HIV, Rabies virus, Influenza virus or Parainfluenza virus. Examples of bacteria are Pseudomonas, Klebsiella, E. coli, Salmonella typhi, Haemophilus influenzae, Bordetella pertussis, Clostridium tetani, or Corynebacterium diphtheriae. An example of a parasite is Plasmodium falciparum.